description. But these are only partial or abstract interpretations, and all merely physical interpretation of our experience is of this partial or abstract character, though in matters of detail we may be, and commonly are, unable to reach a fuller interpretation.

We are accustomed to imagine that, however much our sense-impressions may be tinged with what is only subjective, there is nevertheless a purely objective physical world. In the case of brightness and colour this is a world of electro-magnetic vibrations and their wave-lengths. But the Ängstrom units in which we measure wave-lengths are, no less than the light-years in which we measure the distances of stars or the units in which we estimate their masses, only relative in themselves. It is only because we can refer them to a visible or otherwise sensible standard, such as a centimetre or a gram appears in ordinary life, that they appear to us as real. It is the same with measurements of velocity, as was shown by the famous experiments of Michelson and Morley. Nature only mocks at us, as she seemed to mock at them, when we try to demonstrate a physical universe independent of experience of it. We are thus, as Berkeley pointed out, driven back on sense-experiences and all that they imply, for a criterion of reality, so that a physical world out of relation to them is only an abstraction. A gigantic petitio principii was involved in Galileo's separation of subjective from objective.

We can nevertheless say that biological interpretation can only be extended through the preliminary asumption of self-existent entities or events capable of quantitative, and therefore mathematical, treatment. It is only through the experimental demonstration of inadequacy in provisional physical treatment of brightness, colour, and other sensory experiences that we are led to biological interpretation of them. It seems clear to me that in this sense the extension of physiological or biological interpretation is always based on provisional or superficial physical interpretation, whether we are dealing with the physiology of the senses or with any other part of biology. It is only, for instance, by measurement of what for the moment can be treated as self-existent differences in brightness and colour that we arrive at a physiological interpretation of Weber's law, and of so-called contrast phenomena generally. My own recent detailed study of this subject originated in photometric measurements of the brightness and colour of miners' lamps.

When we look in a still wider manner at our experience we find that all of what we see or otherwise apprehend belongs to a world any part of which implies reference to the other parts in both temporal and spatial order. Thus awareness or perception of this universe implies both memory and imagination, reaching out over both the temporal and spatial order, and not localizable within it. But when we consider what memory and imagination imply we find in what calls itself up in memory or imagination an expression of our interest, or of the co-ordinated and actively persistent whole which each of us calls his personality, and refers his conscious actions to. Ultimately, therefore, sense-experiences are manifestations of personality. Psychology regarded as a science deals with personality. If we neglect the psychological aspect of our experience we are dealing with a relatively abstract or imperfect aspect of it, just as we are doing when we neglect the biological aspect; and the biological aspect itself is only an abstraction from the psychological aspect. But if our universe is an expression of personality, it does not follow that this is mere individual personality. Were it so, science, beauty, and goodness would be merely subjective and fleeting. Actually they appeal to all men. For religion it is the all-pervading personality of God that is revealed in this appeal, and that is the ultimate guarantee of reality. Mathematical, physical, biological, and psychological knowledge are all divine revelations of reality, but in different degrees of incompleteness. It seems to me that in the religious conception of the universe as a progressive manifestation of eternal and omnipresent divine personality we reach what gives a measure of reality to every stage of interpretation.

In a scientific discourse it is usually neither necessary nor customary nowadays to make any reference to religion, but the questions raised in this address are so far-reaching that it might perhaps appear as if I were throwing doubt on the existence of a real and orderly universe. This is far from my intention. We find what is both real and orderly in our universe. It seems to me, however, that we can only realize this ultimately when we realize that it is a spiritual universe. Only then does it appear as real, and not, like the universe which is merely interpreted physically, a universe of artificial abstractions from their underlying reality.

THE KETOGENIC DIET IN THE TREATMENT OF INFECTIONS OF THE URINARY TRACT

WITH A REVIEW OF SIXTEEN CASES

BY

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The treatment of infections of the urinary tract is still far from satisfactory. Only by rendering the urine bacteriologically sterile can success be claimed. It is especially important in such cases to distinguish between drugs which sterilize the urine and those which merely inhibit the growth of the organisms. It is comparatively easy, especially in cases of acute infection, to relieve the symptoms completely, and even to render the urine clear and apparently normal in character. The recovery may be so complete as to suggest to the clinician that the remedy he has prescribed is a disinfectant in the true meaning of the term, and yet, when examined bacteriologically, the urine is swarming with organisms. The acute case offers the greatest chance of success, and treatment should be continued until complete sterilization is achieved, irrespective of whether there are symptoms present or not. With the chronic case one must be prepared to persist with treatment for months on end if necessary, since the complete eradication of the infection is the only safeguard against recurrence of the symptoms. The large number of drugs in use to-day, and the common practice of changing the course of treatment from time to time, are alike a confession of the weakness of our resources against such infections. There is no drug, and no combination of drugs, which can be termed the ideal urinary antiseptic, and there is no means of determining what type of case is likely to prove successful or not except by trial. In these circumstances any new method of treatment of infections of the urinary tract, provided it is based on sound principles, is certainly worthy of thorough and prolonged investigation.

It is now generally agreed that the reaction of the urine is a very important point in urinary antiseptics, and many of the drugs in common use to-day owe their action almost solely to their property of rendering the urine acid. The acidifying power of various drugs—for example, ammonium chloride, ammonium phosphate, etc.—as indicated by the hydrogen-ion concentration of the urine, has now been worked out thoroughly. Scott,[1] Scott and Mitchell,[2] and J. M. Johnston[3] have conclusively shown that, despite a considerable degree of acidity obtained in the urine, the effect on the organisms was practically negligible. Kelsted and Schiodt[4] also found

no sterilizing power in urines which were merely highly acidified. The addition of hexamine is a routine practice, the urinary acidity being essential, since the hydrolysis of hexamine is wholly a function of the hydrogen-ion concentration of the urine (De Eds).[5] A measure of success is obtained with this treatment, but the combination of hexamine with an acidifying agent is apt to give rise to bladder irritation and even haematuria.

HISTORICAL

The ketogenic diet in the treatment of infections of the urinary tract was first tried in 1931 in America by A. L. Clark[6] and H. F. Helmholz[7] working independently. Their aim was physiologically to produce urine of so high acidity as to destroy infecting organisms or to inhibit their growth. This was achieved by providing a diet high in fat and comparatively low in protein content, with a minimum of carbohydrate—resulting in the appearance of acetone and diacetic acid in the urine. In one direction the idea was based on the findings of W. M. Clark[8] in his researches on the final hydrogen-ion concentrations of *B. coli* cultures—namely, *p*H 4.64 to 5.16—which were later substantiated by the work of Shohl and Janney[9] on urines of artificial hydrogen-ion concentration. But the assumption that the lowering of the urinary *p*H by this method would be effective without the addition of a disinfectant was against the weight of opinion and experimental evidence that therapeutically mere acidity does not cause sterilization. With regard to this point it is interesting to note that Helmholz,[10] one of the original observers, had stated emphatically four years previously that, despite the acidity produced in the urine—that is, with drugs—sterilization could not be obtained without the administration of sufficient methenamine. Subsequently, Helmholz[7] reported nine successful cases, three of which had anomalies of the urinary tract. Clark[6] published his findings in fifty cases treated with ketogenic diet. Of the fifty cases treated 66 per cent. were successful and 34 per cent. were unsuccessful, failure being regarded when sterile cultures were not obtained. Both observers were agreed that, in addition to low urinary *p*H values, the presence of ketone bodies was essential. Clark had shown that the presence of ketone bodies without low urinary *p*H was ineffective, but when the *p*H was lowered by the administration of ammonium nitrate the urine had a pronounced bactericidal action. By laboratory experiment Helmholz ruled out diacetic acid and sodium diacetate as the germicidal agent, and in conclusion he stated that "acidity in synergy with substances hitherto not determined probably accounts for the bactericidal action of 'ketonurine.'" Dick's[11] conclusions were similar. More recently A. T. Fuller[12] has shown that the principal inhibitory factor is laevorotatory β-oxybutyric acid, and that its activity increases in proportion to the acidity of the urine.

THE KETOGENIC DIET

The essential features of the ketogenic diet have already been mentioned. In order to avoid any untoward gastric upset following the sudden change of diet, a system of increasing by stages the fatty acid or ketogenic elements in the diet, at the expense of the anti-ketogenic elements, has been adopted. A similar practice is the routine in this method of treatment of epilepsy; and a modified scheme was employed by Clark in his work on urinary sepsis. Numerous schemes are given in the literature on epilepsy, and I have adopted that suggested by F. E. Warner[13] of New York, with some modifications which have proved useful.

The correct ketogenic-anti-ketogenic or F.A./G.L. ratio is too unwieldy a factor to be employed as a basis of calculation as a routine, owing to the fact that the protein, and to a less extent the fat, are made up of both ketogenic and anti-ketogenic elements. In this scheme all the fat is estimated as ketogenic and all the protein anti-ketogenic: and hence, for simplicity, the F.A./G.L. ratio is considered as: $\frac{\text{all the fat}}{\text{the sum of carbohydrate and protein}}$ weighed in grams. When the two factors are compared the error is so small as to be almost negligible from a clinical point of view.

For each diet the weight of the patient is taken and the necessary number of calories estimated. The total calories are estimated at about 50 per cent. above the basal requirement; for each kilogram of body weight 40 to 45 calories are allowed. The number of grams of protein, carbohydrate, and fat is calculated by application of a simple formula, by which the amounts of the three substances can be found readily and altered when the F.A./G.L. ratio is increased. Each gram of carbohydrate and each gram of protein equals 4 calories, and each gram of fat equals 9 calories. It is customary to allow 1 gram of protein for each kilogram of body weight, and the protein content remains constant irrespective of the F.A./G.L. ratio. The number of grams of protein being fixed, the next step is to calculate the number of grams of carbohydrate and fat. If F, C, and P represent the number of grams of fat, carbohydrate, and protein respectively, then:

$$(1)\ 9F + 4(C + P) = \text{total calories.}$$

For a diet of F.A./G.L., ratio 3:1, then:

$$(2)\ F : C + P = 3 : 1.$$

Let $x = C + P$, then:

$$F : x = 3 : 1$$
$$\therefore F = 3x.$$

Applying equation (1):

$$9F + 4x = \text{total calories.}$$

But $F = 3x$,

$$\therefore 31x = \text{total calories}$$
$$\therefore x = \frac{\text{total calories}}{31}$$

This gives the number of grams of fat and the sum of the carbohydrate and protein. But since the number of grams of protein is known, the carbohydrate is found by subtraction: $x - P = C$.

An example will illustrate more clearly.

Weight of patient = 142 lb. = 64 kilos. Allowing 40 calories per kilo, total calories = 2,560.

$$\therefore P = 64 \text{ grams.}$$

Let F.A./G.L. ratio = 3:1

$$\therefore F : C + P = 3 : 1$$
$$\therefore F = 3(C + P)\ ;\ \text{or } F = 3x \text{ where } x = C + P$$
$$\therefore 9F + 4x = 2{,}560$$
$$\therefore 31x = 2{,}560, \text{ since } F = 3x$$
$$\therefore x = 83 \qquad \therefore C + P = 83$$

Since $P = 64$, $C = 83 - 64 = 19$

Since $F = 3x$, $F = 249$

$$\therefore F = 249\ ;\ C = 19\ ;\ P = 64.$$

Diets of different ratio can be easily calculated by substituting the desired ratio in equation (2) above. For example: F.A./G.L. ratio 3.5 : 1, then F : C + P :: 3.5 : 1, the equation being worked out similarly to the one quoted above.

After a little practice the diets are easily handled, and by this method one has a fairly accurate idea of the actual ratio the patient is receiving. Occasionally one finds that the patient cannot take the full diet, or that the diet is not sufficient. In such cases one can alter the total caloric value of the diet without altering the ratio. It is an advantage in some cases to have a high total caloric value of the diet in the higher ratios, since it permits of giving a few more grams of carbohydrate in the diet.

SPECIMEN DIET

A specimen diet is quoted in which the range of items is limited to those on the ordinary hospital menu. It was found necessary to make up the fat content by giving olive oil in emulsion form owing to the expense of cream and butter at the present time. It is not to be recommended if other substances are available, since I have often found that

any nausea that has occurred has done so shortly after taking the olive oil. On the other hand, it illustrates what can be accomplished without the aid of special facilities and with a minimum of expense.

Patient's weight = 142 lb. = 64 kilos. Allowing 45 calories per kilo, total calories = 2,880.

F.A./G.L. ratio = 3.5 : 1

∴ F in grams = 283, C in grams = 17, P in grams = 64.

Olive oil 3 ounces in half-ounce doses = F in grams = 84 and 756 calories.

∴ As diet	F=199	C=19	P=64	Total calories 2,124
	Grams Fat	Grams Carbohydrate	Grams Protein	Total Calories
BREAKFAST:				
2 oz. bacon...	36	0	6	348
1 egg	6	0	6	78
½ oz. energen bread ...	0	1	0	4
1½ oz. butter	34.5	0	0	310
1 oz. milk	1	1.2	1	19
Tea (no sugar).				
DINNER:				
4 oz. chicken	4	0	24	132
1 oz. energen bread ...	0	2	0	8
1½ oz. butter	34.5	0	0	310
4 oz. cream	24	4	4	248
½ oz. almonds	7	2	2.5	81
TEA:				
Tea, with 1 oz. milk ...	1	1.2	1	19
3 oz. fish	0	0	15	60
1 oz. energen bread ...	0	2	0	8
1½ oz. butter	34.5	0	0	310
SUPPER:				
3 oz. cream...	18	3	3	186
	200.5	16.4	62.5	2,121

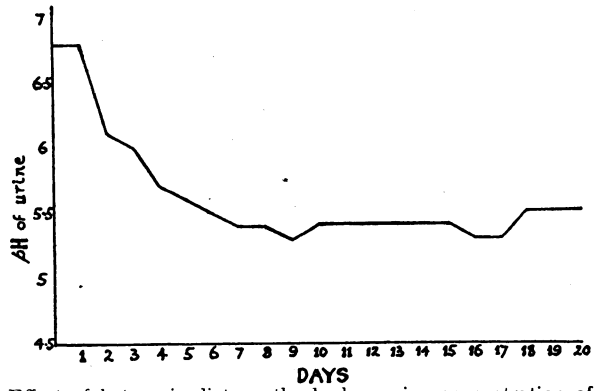
∴ F.A./G.L. ratio = 284.5 : 78.9 = 3.6 : 1 approximately.

As the diet is staged up it becomes increasingly difficult to vary the items. It is important to note that milk cannot be given in any quantity, since it contains almost equal amounts of protein, carbohydrate, and fat, and patients have frequently complained that they are not receiving sufficient. With regard to fluid intake, I have followed the recommendation of Cabot[14] in giving roughly the normal amount. An excess of fluid would be followed by an excess of urinary excretion, with consequent raising of the *p*H and dilution of the ketones.

This method of calculating and handling the diet has worked well in practice. The desired results were produced and maintained in the urine, and at the same time no trouble was caused by nausea and vomiting. I have found the following scheme of value. On the first day a diet ratio of 2 : 1 was given ; if that was well tolerated the diet ratio was increased to 3 : 1 on the following day. This diet was given for two days, since it was found that the urinary *p*H was now low and that acetone was present. On the fourth day the diet was increased to 3.5 : 1 in order to be certain that the *p*H would fall as far as possible, and also to prevent the small rise in the *p*H which had been observed in a few cases to follow the initial sharp fall. This increase also ensured a satisfactory production of acetone bodies where possible. By this method the urinary *p*H was brought down as low and as rapidly as possible, the lowest level being reached in nearly every case by the fifth day, although in some cases even sooner. I have not found it of any advantage to increase the diet ratio above 3.5 : 1. In only a single case was there any complaint of nausea and vomiting, while in several cases which suffered from chronic constipation the condition was entirely relieved. The patients were got up and allowed to walk about the ward as soon as they were considered fit.

The daily examination of the urine for acetone bodies and the estimation of the urinary *p*H are, of course, essential. With regard to the latter, the colorimetric method in a simple comparator is sufficiently accurate for clinical purposes, and with a little practice a series of urines can be examined in a short time. A range of indicators from *p*H 7.4 to *p*H 4.6 is desirable. Daily culture of the urine is desirable, although fairly good results can be obtained by culture twice a week. A single sterile culture is insufficient evidence of sterility, since occasionally growth has been obtained in a later culture. If cultures are sterile on three occasions, especially if spread over a period of a few days, success of the treatment can be claimed.

The effect on the urinary *p*H is well demonstrated in the composite graph prepared from the readings obtained in ten of the cases. All these cases were taking the diet well and were receiving no drugs during that period: there were no factors present—for example, intercurrent acute conditions—which might have given rise to abnormal



Effect of ketogenic diet on the hydrogen-ion concentration of the urine.

metabolism. The average urinary *p*H of these cases was taken before the diet was started: the average of the daily *p*H values was calculated for the first twenty days. All were cases of *B. coli* infection. It is noted that there was a sharp initial fall in the urinary *p*H, the low general level of *p*H 5.4 being reached on the seventh day. In individual cases there was some evidence to show that the fall was more rapid in cases in which the fat ratio of the diet was increased more quickly. After the initial fall the *p*H assumed a general level lasting about eighteen days, when there was a slight rise. This slight rise in the two final readings is of some importance, since it was invariably noted that towards the end of the third week of treatment the general trend of the *p*H rose, assuming a slightly higher level and tending to become more irregular. When the diet was not being followed strictly the result was clearly reflected in the *p*H graphs: in two such cases (Cases 10 and 11) the *p*H was more irregular than in any of the others. In another two cases, in which the value was about *p*H 6 before treatment was started, there was a fall to *p*H 5.1, which indicated that this diet had the power to render more acid urine which was already well on the acid side of neutrality—always a very difficult and uncertain operation.

PRODUCTION OF ACETONE BODIES

In every case treated with diet of high ketogenic ratio acetone bodies were produced in the urine, but in varying quantity in individual cases. The production of acetone was greatest during the first five days following the fall of the *p*H, but began to diminish in about ten days, and by the end of the third week had become scanty, in some cases only traces being demonstrable. These findings, together with the fact that the *p*H tended to rise after three weeks, appeared to show that the body was adjusting itself to the abnormal metabolism. There was no fixed relation between the *p*H and the amount of acetone present. In one case (Case 2) the *p*H never fell below 5.7, but an abundance of acetone was demonstrated over a

period of eight days. On the other hand, in Case 6, although the general level of the *p*H remained considerably lower—namely, *p*H 5.3—acetone was always scanty, never more than a trace being found.

STERILIZING EFFECT OF DIET

Sixteen cases of infection of the urinary tract were treated with ketogenic diet. Five of these were cured completely with no other treatment; five were cured completely with diet and drug treatment combined; in one case the result was left doubtful, since only a single final culture was proved sterile. Cases were regarded as cured when urinary cultures were repeatedly sterile. Of the five cases which failed, three left hospital before treatment was completed; one failed completely to take the diet; and one was suffering from chronic pyonephrosis, which, during treatment, showed acute exacerbations upsetting metabolism and interfering with the treatment.

TABLE OF RESULTS

Case	Diagnosis	Organisms	Duration	*p*H General Level	Ketonuria	Combined Drug Therapy	Result	Days Required	Remarks
1. E. L. ...	Pyelocystitis	*B. coli*	3 weeks	5.3	Satisfactory	—	Sterile	34	—
2. F. G. ...	Pyelitis	„	3 years	5.7	Good	—	„	6	—
3. A. D. ...	Cystitis	„	3 years	5.3	Good	—	„	17	Probably sterile on fourteenth day
4. M. C. ...	Pyelitis	„	5 months	5.4	Satisfactory	—	„	27	Solitary kidney
5. F. C. ...	„	„	2 months	5.3	Good	—	„	8	—
6. E. H. ...	„	„	14 days	5.3	Poor	Amm. nit.	„	25	Poor ketonuria
7. M. J. ...	Pyelocystitis	„	8 years	5.4	Satisfactory	„	„	23	*p*H irregular
8. D. G....	Pyelitis	*B. coli* and staph.	Indefinite	Irregular	Traces irregular	„	„	25	Not taking diet. *B. coli* sterile fourteenth day
9. J. W. ...	„	Staph.	3 years	Irregular	Poor	„	? Sterile	21	Single culture
10. C. B....	Pyelocystitis	*B. coli*	2 years	5.4 rising	Poor	Hexamine	Sterile	40	Poor acetone. Sterile tenth day
11. E. W...	Pyelitis	„	14 days	—	Poor	„	„	49	—
12. H. C....	„	*B. coli* and staph.	4 months	5.4 irregular	Poor	—	*B. coli*, unsterile Staph., sterile	—	Culture once sterile, then *B. coli* recurred. Left hospital
13. M. W...	Pyelocystitis	*B. coli*	5 months	5.5	Good	—	Unsterile	—	Improved. Left hospital
14. J. D....	Pyonephrosis	„	3 years	Irregular	Poor	—	„	—	Subacute condition; acute attacks
15. L. B....	Pyelitis	„	8 months	5.3	Satisfactory	—	„	—	Improved. Left hospital
16. E. D...	Pyelocystitis	„	6 weeks	6.8	None	—	„	—	Failed completely to take diet

Of the five cases sterilized by diet the figure had been maintained constantly at a low level—namely, *p*H 5.4 or lower; but in one case the *p*H was 5.7. All of them showed a satisfactory acetone reaction daily. The number of days on diet before the first sterile culture was obtained varied from eight to thirty-four days, but there was no relation between the chronicity of the infection and the time taken for sterilization—for example, Case 2, of three years' standing, cleared up in six days, while Case 1, of only three weeks' standing, took thirty-four days on treatment before the urine became sterile. Cases 6 and 7 became sterile after ammonium nitrate had been given. In both these cases the *p*H tended to rise after three weeks on treatment, and the ammonium nitrate overcame this tendency. In the second of these cases the *p*H had been irregular, but acetone bodies had been present in considerable amount, even when the urinary figure was *p*H 6. It is important to note that in both these cases, although the *p*H was steadied and slightly lowered by the administration of ammonium nitrate, no increase in the amount of acetone bodies was demonstrated. The two cases which were given hexamine were to be regarded as partial failures. The *p*H had been satisfactory, generally about *p*H 5.4, but acetone production was poor throughout. Since the *p*H was comparatively low the administration of hexamine appeared a reasonable procedure, as the hydrolysis of hexamine is entirely a function of the hydrogen-ion concentration. Both cases were sterile after ten days on hexamine treatment. Although the urinary *p*H was low, and free formaldehyde was demonstrable in the urine, there was no complaint of irritability of the bladder nor other untoward symptoms which have frequently accompanied hyperacidity of the urine and free formaldehyde obtained by the administration of drugs.

The last case reported was of some interest. Although given a diet of comparatively low fat ratio, severe nausea and vomiting occurred, and after two days the diet had to be stopped.

EFFECT ON SYMPTOMS AND URINE

In every case treated there was a very marked improvement in the symptoms and in the characters of the urine. By the end of the first week the symptoms had improved markedly, scalding of the vulvae, if present, generally being the first to disappear. In a fortnight's time complaints were few. Loin pain and tenderness had disappeared; a number of patients still complained of frequency, although this feature was also alleviated. The improvement in the characters of the urine was almost equally marked. By the end of fourteen days most of the urines were clear in a tall flask, with only a trace of deposit. Two cases which had cloudy urines within an inch of "pussy" deposit cleared completely in a week. In not a single case was there any complaint of irritability of the bladder due to the hyperacid urine, even in the two cases which were receiving hexamine. These findings are of considerable importance. Two cases were nursing mothers. Samples of milk showed normal carbohydrate and fat contents, while in neither case did the child suffer any gastro-intestinal symptoms which might have been attributed to abnormal composition of the milk. Both babies were healthy, and their weights increased at the normal rates. Chronic infection of the urinary tract sometimes succeeds the pyelitis of pregnancy; the fact that the child is on breast-feeding is no contraindication to the ketogenic diet. A few patients tended to put on weight, but every case without exception was in excellent health on discharge from hospital, a fact which must not be overlooked. It was found necessary to explain to the patients that nothing should be eaten except what was

given to them, and in most cases there was no difficulty in obtaining their strict co-operation. It was usual also to inform them before starting that the treatment was likely to take some time before good results could be expected.

The investigation of these sixteen cases showed that ketogenic diet is an unsuitable form of treatment for out-patients. Accurate preparation and administration of the diet was essential if the urinary *p*H was to be kept steadily at low levels. Two patients who were not taking the diet strictly, and which would be representative of the average out-patient receiving treatment without supervision, produced very irregular and high *p*H values, which were not contributive to success.

CONCLUSIONS

Sixteen cases of infection of the urinary tract treated with ketogenic diet are discussed.

1. Ketogenic diet had the effect of increasing the hydrogen-ion concentration of the urine in all cases except one. The effect on the urinary *p*H was characterized by a rapid initial fall, and a maintained low general level lasting till the end of the third week, when there was a tendency for the *p*H to become irregular and to stand at a slightly higher level.

2. Acetone bodies were produced in the urine in all cases, but varying greatly in amount in individual cases. Acetone appeared in greatest amount during the first five days after the *p*H had fallen, and by the end of three weeks had become very much diminished.

3. Five cases were cured completely by treatment with ketogenic diet. In these cases the urinary figure was maintained about *p*H 5.4 and acetone bodies were produced in satisfactory quantity. Four cases were cured following the addition of ammonium nitrate to the treatment. Two cases were cured following the addition of hexamine to the treatment. Five cases were improved, but the urines were not sterile. Of these, three left hospital before treatment was completed ; one was suffering from a subacute condition which interfered with metabolism ; and one failed completely to take the diet.

4. Treatment with ketogenic diet improved the symptoms and the characters of the urine rapidly. No symptoms were caused by the hyperacid urine.

5. It was found desirable to increase the diet by stages according to the ketogenic-anti-ketogenic ratio, in order to avoid nausea and vomiting. Only a single case had any gastric upset.

6. Two cases were nursing mothers. The milk was found to be of normal composition, and no gastro-intestinal symptoms were shown by the babies.

7. Every patient was in excellent health on discharge from hospital.

8. The results suggested that ketogenic diet was an unsuitable form of treatment for out-patient departments.

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ERYTHEMA NODOSUM

BY

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Three divergent views are to be found in the literature regarding the aetiology of erythema nodosum.

1. *The Rheumatic.*—Following the work of Mackenzie[1] some fifty years ago the theory that erythema nodosum was associated with the acute rheumatic process was formulated. This view was supported by clinical evidence which showed that certain cases of the disease were preceded by acute tonsillitis of the streptococcal type, associated with polyarthritis and sometimes followed by rheumatic valvular disease of the heart. The exact relation was never clearly defined. However, this view got into the English textbooks, where it has remained until the present day.

2. *The Tuberculous.*—For many years Continental workers have called attention to the fact that certain cases of erythema nodosum are closely associated with tuberculosis. Recently, due chiefly to the careful work of the Scandinavian school—particularly to the researches of Wallgren[2] and Ernberg[3]—the connexion between the disease and tuberculosis has been largely explained. These workers have shown that the great majority (95 per cent.) of patients with erythema nodosum are strongly positive to tuberculin, that tubercle bacilli may be found by the gastric lavage method in a high percentage of cases, that *x*-ray skiagrams of the chest reveal primary lung and hilus lesions in the majority of cases, and that a fair number of patients who have suffered from the disease develop frank tuberculous lesions within a year of the attack. They consider that erythema nodosum is a manifestation of primary tuberculous infection, such as phlycternular conjunctivitis, " benign infiltration of the lung," and early pleurisy, which conditions they term " paratuberculous."

3. *The Acute Specific Disease.*—Neither the rheumatic nor the tuberculous school have ever been able to claim all the cases ; hence Trousseau,[4] Lendon,[5] and Symes[6] put forward the view, at different times, that the disease was essentially an acute specific fever. Their arguments were plausible, and many were inclined to accept their views, including such careful clinical observers as Robert Hutchison. Their theory was based, however, on mere deduction, and was supported by no experimental evidence. A variation of this view was put forward more recently by Fornara,[7] who suggested that the disease was caused by a specific virus, but that the actual eruption only occurred when the patient was in a state of allergy to the tubercle bacillus.

AUTHOR'S OBSERVATIONS

Some two years ago I[8] published the result of certain investigations which had led me to conclude that " erythema nodosum is a type of hyper-reactive tissue response to different bacterial allergens, and that the allergens responsible for the disease in London are commonly tuberculin and haemolytic streptococcal endotoxin." The table given below, and reprinted, with permission from the *Quarterly Journal of Medicine*, gives in the briefest space the facts upon which this deduction was made.

The cases are seen to fall into two groups. The first five belong to the tuberculous type, the latter three to the streptococcal or rheumatic type. In the first group